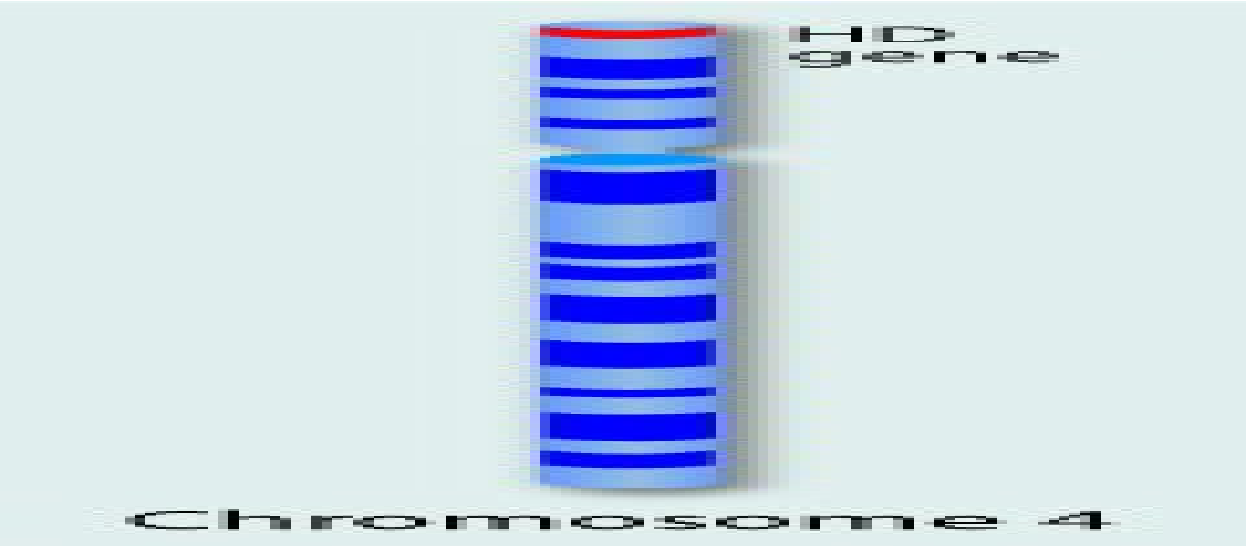
BIOL1010A
Assignment #2
Genetic Disease Briefing

Araz Amini
100948062
Mr.Cheetham
08/11/13

Huntington's Disease



Huntington disease is an inherited neurodegenerative genetic disorder that dysfunctions/declines one's cognition, movement and leads to mental disturbances, including depression and altered personality. The disease is particularly seen in humans aged 35-45 years, although 5-10% of juvenile variant can be affected. The disease is an autosomal dominant mutation, therefore the offspring of the affected parent with Huntington Disease has a 50% of inheriting the disease-

causing allele. Huntington disease is commonly seen in those of European descent and it affects 0.0001% of the population. The HTT gene that codes for huntingtin is caused by a trinucleotide repeat expansion (CAG), about 36 or more repeats in the gene, although it is a very low spontaneous mutation rate. The trinucleotide repeat expansion (CAG) is the only known mutation associated with the gene. The glutamine repeat expansion occurs at the beginning (N terminus) of huntingtin. The gene is located on the short arm of chromosome 4, specifically at position 16.3, from base pair3,113,411 to base pair 3,282,655. Normal levels in huntingtin is essential for normal brain development in both humans and animals. Huntington is associated with neurogenesis, the process of neural generation, it binds to nerve growth factors to regulate neural transcription. Huntington acts on neurons of the brain and peripheral nervous system. Huntington is plays a role in protecting against neural apoptosis. As a result of Huntington Disease, its role is countered as the increase in the length of the CAG segments (polyglutamine) that leads to a mutant (longer) huntington protein. The repetitive elongation of the protein is cut, resulting in toxic fragments that bind together and accumulate in neuron. This disrupts the cell's normal function, hence prohibiting the gene to act normally. The expansion's increase determines the severity of the disease, and its increase results in more severe symptoms which progressively get worse through generations.

Signs of Huntington disease are classified in the early,middle and late stage of the disease. In the early stages, the onset psychiatric disorders are more prominently seen, such as hallucinations, depression and anxiety. As the disease progresses, commonly through the onset of age, one develops movement dysfunctions. Chorea, an abnormal involuntary motion, results from Huntington disease and is prominent sign in HD victims. Also, declines in reaction and inability

to control normal motion. In late stages, cognition and movement become intertwine in a negative manner, for instance, an increase in chorea among the inability to pronounce words or even talk. Bradykinesia, the inability to move normally, or move at all, is also an early stage in Parkinson's. Diagnosis of Huntington's disease is frequently observed in the affected family's history considering the disease is autosomal dominant. Also a physician will prominently seen an increase in abnormal movement, classified as chorea. Testing can be done through allele- specific mutation analysis, a genetic method of testing for the abnormal nucleotide repeat expansion, to figure out whether the glutamine repeat is greater than 36 in the gene. Also, there are many diseases similar to Huntington disease which may exhibit similar biochemical/genetic properties. Through differential diagnosis, a physician test for Huntington disease-like compared to Huntington disease through the process of elimination. Other means of testing can be done with MRI machines to depict the area of weakness in the brain (frontal lobe) associated with the disease.The effects of Huntington disease can be treated through suppression with drugs. Chorea can be suppressed by neuroleptic drugs such as benzodiazepines and olanzapines. Bradykinesia can be suppressed through the use of dopamine(DA) increasing drugs such as apomorphine. Other mental disorders such as depression can be treated with psychiatric drugs.

Genetic counselling, process of providing individuals and families with information on the nature, inheritance, and implications of genetic disorders, is a notable aspect in determining the risk for affected families. Prenatal testing is essential in determining whether the progeny will have the disease. In prenatal testing, DNA is extracted from the fetus during pregnancy and is examined in vitro to confirm whether the fetus will have the disease. Genetic counsellors

conclude that the onset of the disease may not been seen in family history due to failure in recognizing it in a family member whether the affected died whilst having the disease before the onset of symptoms or the repeat is slightly below abnormal resulting in less than complete penetrance. Also, if the affected parent is male, the offspring is slightly more prone to inherit the disease, and a counsellor will discuss the greater possibilities of a male parent having the disease with the affected family. Sometimes, a victim of the disease may be asymptomatic, showing no signs or symptoms, and are tested through prediction methods by analyzing family history. A genetic counsellor can set appointments for the affected families to test for potential disease inheritance in the family. When Huntington disease, or any disease is afflicting on the family, the family is impacted psychosocially. There are therapeutic implications for the affected families. Affected families can attend support groups through programs by the Huntington's Disease Association. Huntington disease doesn't only affect the victim, but it affects the family of the victim. Affected families have trouble coping with affected person, through the unmanageable effects of the disease that may be disturbing for them. They are sensitive to shifts in that person's personality or their physical motions. A system was proposed by Dr. Murray Bowen, known as the Family System Theory. This system relies on the aspect of mutual help, in an all-for-one effort in helping the affected person cope with their lives.

Overall, Huntington disease impacts the disease-inherited victim as well as their family. Huntington disease is studied by physicians to further the knowledge of the disease and to look for potential treatments. Huntington disease is studied by genetic counsellors to provide the knowledge for the affected families and to understand the potential risk of the disease in affected families.

Warby SC, Graham RK, Hayden MR. Huntington Disease. 1998 Oct 23 [Updated 2010 Apr 22]. In: Pagon RA, Adam MP, Bird TD, et al., editors. GeneReviews™ [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2013. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1305/ “process of providing individuals and families with information on the nature, inheritance, and implications of genetic disorders”

Smolina, Ekaterina.*Psychosocial impact of Huntington's disease on families and spouses from the perspective of the Family Systems Theory*. Diss. 2007. Print. <https://journal.lib.uoguelph.ca/index.php/surg/article/view/338/456>.

"HUNTINGTON DISEASE; HD."*http://www.omim.org/entry/143100?search=huntington disease&highlight=huntington disease*. OMIM® and Online Mendelian Inheritance in Man, 10 february 2013. Web. 11 Nov 2013. “ at position 16.3, from base pair3,113,411 to base pair 3,282,655”

"HTT." *Genetics Home Reference*. U.S. National Library of Medicine®, 04 Nov 2013. Web. 11 Nov 2013. <http://ghr.nlm.nih.gov/gene/HTT>. “The elongated protein is cut, resulting in toxic fragments that bind together and accumulate in neurons, disrupting the normal function of these cells, see "HTT" http://ghr.nlm.nih.gov/gene/HTT”

"Huntington Disease clinical." *Neuroscience 410*. N.p., 18 march 2008. Web. 11 Nov 2013. <http://www.canr.ualberta.ca/documents/drwmartinhd_neuroscience410notes.pdf>.

"Huntington Disease." *Genetics Home Reference*. U.S. National Library of Medicine®, n.d. Web. 11 Nov 2013. <http://ghr.nlm.nih.gov/condition/huntington-disease>.

"Huntington's Disease Genetics." *News Medical*. N.p., 11 November 2013. Web. 11 Nov 2013. <"Huntington Disease." Genetics Home Reference. U.S. National Library of Medicine®, n.d. Web. 11 Nov 2013. .>.